

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Attorney Docket No.: ISPH-0520  
Inventors: Crooke et al.  
Serial No.: 09/781,712  
Filing Date: February 12, 2001  
Examiner: Not Yet Assigned  
Group Art Unit: 1635  
Title: Methods of Using Mammalian RNase H and  
Compositions Thereof

I, **Jane Massey Licata**, Registration No. 32,257, certify that this correspondence is being depositing with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents and Trademarks, Washington, D.C. 20231.

On this date: July 5, 2001

Jane Massey Licata  
Jane Massey Licata, Registration No. 32,257

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**INFORMATION DISCLOSURE STATEMENT**

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

(XX) In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into

the national stage of the above identified application as set forth in §1.491, or before the mailing date of a first Office Action on the merits of the above-identified application, no additional fee is required.

- ( ) In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, therefore:

- ( ) Certification in Accordance with §1.97(e) is set forth below; or

- ( ) The fee of \$240.00 as set forth in §1.17(p) is attached.

- ( ) In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); Petition Requesting Consideration of the Information Disclosure Statement; and the fee of \$130.00 as set forth in §1.17(i)(1).

(xx) Copies of each of the references listed on the attached Form PTO-1449 (modified) are enclosed herewith.

- ( ) In accordance with §1.98(d), copies of some or all of the references listed on the attached Form PTO-1449 (modified) are not enclosed herewith because they were previously

submitted to the U.S. Patent and Trademark Office in prior application Serial No. \_\_\_\_\_, filed \_\_\_\_\_, for which a claim for priority under 35 U.S.C. §120 has been made in the instant application.

Please charge any deficiency or credit any overpayment to Deposit Account No. 50-1619. This form is submitted in duplicate.

( ) The relevance of the listed references in a foreign language is as stated in the specification at pages @@.

(XX) All listed references are in the English language.

Respectfully submitted,

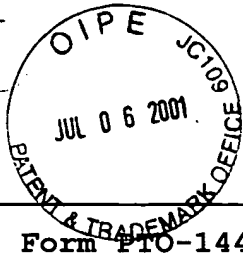


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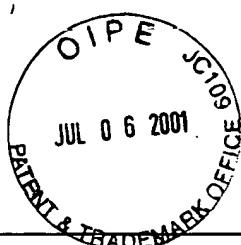
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<b>Form PTO-1449 Modified</b>		Docket No. <b>ISPH-0520</b>	Serial No. <b>09/781,712</b>
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce		Applicant <b>Crooke et al.</b>	
		Filing Date <b>February 12, 2001</b>	Group <b>1635</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	AA	Agrawal, et al., "Site-specific excision from RNA by Rnase H and mixed-phosphate-backbone oligodeoxynucleotides", <i>Proc. Natl. Acad. Sci. USA</i> <b>1990</b> 87:1401-1405	
	AB	Boado et al., "Complete Inactivation of Target mRNA by Biotinylated Antisense Oligonucleotide-Avidin Conjugates", <i>Bioconjugate Chem.</i> <b>1994</b> 5:406-410	
	AC	Bordier et al., "Sequence-specific inhibition of human immunodeficiency virus (HIV) reverse transcription by antisense oligonucleotides: Comparative study in cell-free assays and in HIV-infected cells", <i>Proc. Natl. Acad. Sci. USA</i> <b>1995</b> 92:9383-9387	
	AD	Büsen et al., "Distinct Ribonuclease H Activities in calf Thymus", <i>Eur. J. Biochem.</i> <b>1975</b> 52:179-190	
	AE	Büsen et al., "Ribonuclease H Levels during the Response of Bovine Lymphocytes to Concanavalin A", <i>Eur. J. Biochem.</i> <b>1977</b> 74:203-208	
	AF	Büsen W., "Purification, Subunit Structure, and Serological Analysis of Calf Thymus Ribonuclease H I*", <i>J. of Biol. Chem.</i> <b>1980</b> 255(19):9434-9443	
	AG	Büsen W., "The Subunit Structure of Calf Thymus Ribonuclease H I As Revealed by Immunological Analysis", <i>J. Biol. Chem.</i> <b>1982</b> 257(12):7106-7608	
	AH	Cazenave et al., "Comparative inhibition of rabbit globin mRNA translation by modified antisense oligodeoxynucleotides", <i>Nuc. Acids Res.</i> <b>1989</b> 17:4255-4271	
	AI	Cerritelli et al., "Cloning, Expression, and Mapping of Ribonucleases H of Human and Mouse Related to Bacterial Rnase HI", <i>Genomics</i> <b>1998</b> 53:300-307	
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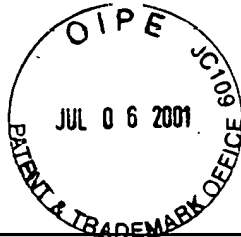


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	AJ	Chiang et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms", <i>J. Biol. Chem.</i> <b>1991</b> 266(27):18162-18171	
	AK	Crooke et al., "Kinetic characteristics of Escherichia coli RNASE H1:cleavage of various antisense oligonucleotide-RNA duplexes", <i>Biochem.</i> <b>1995</b> 312:599-608	
	AL	Crouch et al., "Ribonucleases H", <i>Nuclease Linn and Roberts, Eds. Cold Spring Harbor Laboratory Press, Plainview, NY</i> <b>1982</b> 211-241	
	AM	Dagle et al., "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides:studies of An2 and cyclin in embryogenesis", <i>Nucl. Acids Res.</i> <b>1990</b> 18(16):4751-4757	
	AN	Dash et al., "Selective elimination of mRNAs in vivo:Complementary oligodeoxynucleotides promote RNA degradation by an RNase H-like activity", <i>Proc. Natl. Acad. Sci. USA</i> <b>1987</b> 84:7896-7900	
	AO	Dean et al., "Inhibition of Protein Kinase C- $\alpha$ Expression in Human A549 Cells by Antisense Oligonucleotides Inhibits Induction of Intercellular Adhesion Molecule 1 (ICAM-1) mRNA by Phorbol Esters", <i>J. Biol. Chem.</i> <b>1994</b> 269(23):16416-16424	
	AP	Eder et al., "Substrate specificity of human RNase H1 and its role in excision repair of ribose residues misincorporated in DNA", <i>Biochimie</i> <b>1993</b> 75:123-126	
	AQ	Frank et al., "Purification and characterization of human ribonuclease HII", <i>Nucl. Acids Res.</i> <b>1994</b> 22(24):5247-5254	
	AR	Frank et al., "Cloning, Subcellular Localization and Functional Expression of Human RNase HII", <i>Biol. Chem.</i> <b>1998</b> 379:1407-1412	
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<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	AS	Frank et al., "Cloning of the cDNA encoding the large subunit of human RNASE HI, a homologue of the prokaryotic RNase HII", <i>Proc. Natl. Acad. Sci. USA</i> <b>1998</b> 95:12872-12977	
	AT	Furdon et al., "RNase H cleavage of RNA hybridized to oligonucleotides containing methylphosphonate, phosphorothioate and phosphodiester bonds", <i>Nucl. Acids Res.</i> <b>1989</b> 17(22):9193-9204	
	AU	Gagnor et al., "α-DNA VI: comparative study of α-and β-anomeric oligodeoxyribonucleotides in hybridization to mRNA and in cell free translation inhibition", <i>Nucl. Acids Res.</i> <b>1987</b> 15(24):10419-10436	
	AV	Ghosh et al., "Phosphorothioate-phosphodiester oligonucleotide co-polymers: assessment for antisense application", <i>Anti-Cancer Drug Design</i> <b>1993</b> 8:15-32	
	AW	Giles et al., "Enhanced RNase H activity with methylphosphonodiester/phosphodiester chimeric antisense oligodeoxynucleotides", <i>Anti-Cancer Drug Design</i> <b>1992</b> 7:37-48	
	AX	Giles et al., "Increased specificity for antisense oligodeoxynucleotide targeting of RNA cleavage by RNase H using chimeric methylphosphonodiester/phosphodiester structures", <i>Nucl. Acids Res.</i> <b>1992</b> 20:763-770	
	AY	Godard et al., "Antisense effects of cholesterol-oligodeoxynucleotide conjugates associated with poly(alkylcyanoacrylate) nanoparticles", <i>Eur. J. Biochem.</i> <b>1995</b> 232:404-410	
	AZ	Gottikh et al., "αβ Chimeric Antisense Oligonucleotides: Synthesis and Nuclease Resistance in Biological Media", <i>Antisense Res. Dev.</i> <b>1994</b> 4:251-258	
	BA	Hausen et al., "Ribonuclease H An Enzyme Degrading the RNA Moiety of DNA-RNA Hybrids", <i>Dur. J. Biochem.</i> <b>1970</b> 14:278-283	
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	BB	Hoke et al., "Effects of phosphorothioate capping on antisense oligonucleotide stability, hybridization and antiviral efficacy versus herpes simplex virus infection", <i>Nucl. Acids Res.</i> <b>1991</b> 19(2):5743-5748
	BC	Itaya et al., "Selective cloning of genes encoding RNASE H from <i>Salmonella typhimurium</i> , <i>Saccharomyces cerevisiae</i> and <i>Escherichia coli rnh</i> mutant", <i>Mol. Gen. Genet</i> <b>1991</b> 277:438-445
	BD	Itaya et al., "Molecular cloning of a ribonuclease H (RNase HI) gene from an extreme thermophile <i>Thermus thermophilus</i> HB8: a thermostable RNase H can functionally replace the <i>Escherichia coli</i> enzyme in vivo", <i>Nucl. Acids Res.</i> <b>1991</b> 19(16):4443-4449
	BE	Itaya M., "Isolation and characterization of a second RNase H (RNase HII) of <i>Escherichia coli</i> K-12 encoded by the <i>rnhB</i> gene", <i>Proc. Natl. Acad. Sci. USA</i> <b>1990</b> 87:8587-8591
	BF	Kanaya, et al., "Importance of the Positive Charge Cluster in <i>Escherichia coli</i> Ribonuclease HI for the Effective Binding of the Substrate", <i>J. Biol. Chem.</i> <b>1991</b> 266(18) 11621-11627
	BG	Kanaya et al., "Expression, Purification, and Characterization of a Recombinant Ribonuclease H from <i>Thermus thermophilus</i> HB8", <i>J. Biol. Chem.</i> <b>1992</b> 267(14):10184-10192
	BH	Kane C., "Renaturase and Ribonuclease H: A Novel Mechanism That Influences Transcript Displacement by RNA Polymerase II in Vitro", <i>Biochemistry</i> <b>1988</b> 27:3187-3196
	BI	Katayanagi et al., "Three-dimensional structure of ribonuclease H from <i>E. coli</i> ", <i>Nature</i> <b>1990</b> 347:306-309
	BJ	Katayanagi et al., "Crystal Structure of <i>Escherichia coli</i> RNase HI in Complex with Mg <sup>2+</sup> at 2.8 Å Resolution: Proof for a Single Mg <sup>2+</sup> Binding Site", <i>Proteins: Struct., Funct., Genet.</i> <b>1993</b> 17:337-346
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	BK	Kawasaki E., "Quantitative hybridization-arrest of mRNA in Xenopus oocytes using single-stranded complementary DNA or oligonucleotide probes", <i>Nucl. Acids Res.</i> <b>1985</b> 13:4991-5005	
	BL	Lee et al., "Antisense Gene Suppression Against Human ICAM-1, ELAM-1, and VCAM-1 in cultured Human Umbilical Vein Endothelial Cells", <i>Shock</i> <b>1995</b> 4(1):1-10	
	BM	Lima et al., "Binding Affinity and Specificity of <i>Escherichia coli</i> RNASE H1: Impact on the Kinetics of Catalysis of Antisense Oligonucleotide-RNA Hybrids", <i>Biochemistry</i> <b>1997</b> 36:390-398	
	BN	Lima et al., "The Influence of Antisense Oligonucleotide-induced RNA Structure on <i>Escherichia coli</i> RNase H1 Activity", <i>J. Biol. Chem.</i> <b>1997</b> 272(29):18191-18199	
	BO	Liu et al., "Suppression of Ischemia-induced Fos Expression and AP-1 Activity by an Antisense Oligonucleotide to c-fos mRNA", <i>Ann. Neurol.</i> <b>1994</b> 36:566-576	
	BP	Monia et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression", <i>J. Biol. Chem.</i> <b>1993</b> 268(19):14514-14522	
	BQ	Nakamura et al., "How does RNase H recognize a DNA-RNA hybrid?", <i>Proc. Natl. Acad. Sci. USA</i> <b>1991</b> 88:11535-11539	
	BR	Quartin et al., "Number and distribution of methylphosphonate linkages in oligodexynucleotides affect exo-and endonuclease sensitivity and ability to form RNase H substrates", <i>Nucl. Acids Res.</i> <b>1989</b> 17:7253-7262	
	BS	Rong et al., "On the Molecular Weight and Subunit Composition of Calf Thymus Ribonuclease H1", <i>Biochemistry</i> <b>1990</b> 29:383-389	
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	BT	Rosolen et al., "Effect of over-expression of bacterial ribonuclease H on the utility of antisense MYC oligodeoxynucleotides in the monocytic leukemia cell line U937", <i>Biochimie</i> <b>1993</b> 75:79-87	
	BU	Saison-Behmoaras et al., "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24", <i>EMBO J.</i> <b>1991</b> 10:1111-1118	
	BV	Stein et al., "Enzyme from Calf Thymus Degrading the RNA Moiety of DNA-RNA Hybrids:Effect on DNA-Dependent RNA Polymerase", <i>Science</i> <b>1969</b> 166:393-395	
	BW	Tidd et al., "Evaluation of N-ras oncogene anti-sense, sense and nonsense sequence methylphosphonate oligonucleotide analogues", <i>Anti-Cancer Drug Des.</i> <b>1988</b> 3:117-127	
	BX	Tidd et al., "Partial protection of oncogene, anti-sense oligodeoxynucleotides against serum nuclease degradation using terminal methylphosphonate groups", <i>Br. J. Cancer</i> <b>1989</b> 60:343-350	
	BY	Walder et al., "Role of RNASE H in hybrid-arrested translation by antisense oligonucleotides", <i>Proc. Natl. Acad. Sci. USA</i> <b>1988</b> 85:5011-5015	
	BZ	Wintersberger U., "Ribonucleases H of Retroviral and Cellular Origin", <i>Pharmac. Ther.</i> <b>1990</b> 48:259-280	
	CA	Wu et al., "Molecular Cloning and Expression of cDNA for Human RNase H", <i>Antisense Nucl. Acid Drug Dev.</i> <b>1998</b> 8:53-61	
	CB	Yang et al., "Structure of Ribonuclease H Phased at 2 Å Resolution by MAD Analysis of the Selenomethionyl Protein", <i>Science</i> 249:1398-1405	
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## U. S. PATENT DOCUMENTS

Examiner		Document	Date	Name	Class	Subclass
	AA	6,001,653	12-14-99	Crooke et al.	435	375

## FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES NO	

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